BRAIN Initiative and Human Brain Project: Hopes and Reservations

Multidimensional Brain Space

Silvia Arber
Biozentrum and FMI

Two big international initiatives have the provocative goal to bundle information and to act as a platform for exchange to unravel the mysteries of brain function. Current technical limitations to brain discovery science represent clear-cut entry points for both initiatives. Generation of conceptual breakthroughs in brain science, however, represents the main challenge and reason for excitement. For success, both initiatives will need strong interactions with individual scientists to benefit from in-depth knowledge and biological understanding in their area of expertise. It will only be through this strategy that large data sets will be meaningful and that principles for how the brain works and dysfunctions in disorders can be extracted.

Insight should emerge from mining multidimensional data including the following areas. Diversity: identification of mechanisms translating molecular into functional diversity will help to understand the distinct languages of neuronal subtypes. Space: binding together knowledge on local circuit and long-range computations with neuromodulatory influence will provide an integral view on brain function. Time: understanding the temporal axis of neuronal-cell-type maturation and plasticity will help unravel selective neuronal response profiles in disease. Organism: comparing differences between brains of one species and across species will uncover principles of overarching conservation and divergence in circuit modules.

A Down Payment on the Brain

Michael D. Ehlers
Neuroscience Research Unit, Pfizer, Inc.

The brain has long been fascinating and mysterious, but the science of the brain and nervous system is increasingly critical for social well being. The economic burden of neurological and psychiatric illnesses dwarfs other areas of human disease. Neurodegenerative disease care is poised to consume vast swaths of health care budgets around the globe. Depression remains the single largest cause of disability, adjusted for life years, in the U.S. Stroke remains a major killer. Unfortunately, few new therapies for neuroscience diseases have been developed, and neuroscience research dollars have lagged.

Now with the advent of the Obama/NIH BRAIN Initiative and the EU's Human Brain Project, there is an opportunity to accelerate fundamental brain sciences. The ambitions of both initiatives are grand, but less clear is whether these grand ambitions will be supported by sufficient funds. In the case of the BRAIN Initiative, $100 million (perhaps a bit more) will be targeted to brain science across multiple federal agencies. This compares to the $500-700 million plus required to conduct a single phase 3 clinical development program for one experimental drug in Alzheimer's disease, or the $1.5 trillion or so in annual costs of brain disorders in the U.S. and E.U. combined. It is reassuring that policy leaders are recognizing the need and the opportunity. Beyond this initial down payment, now is the time to invest and resource accordingly.

Big Science Needs New Concepts

Yves Frégnac
CNRS, Unit of Neuroscience, Information and Complexity

As a member of the Human Brain Project (HBP), I am divided between two attitudes. One is optimistic: these two complementary initiatives will yield nonincremental progress in medicine and systems neuroscience. HBP is centered on neuroinformatics and virtual (simulation-driven) medicine; The NIH initiative will provide the essential measures for constraining models.

The other is a thread of doubt: multiomic research will create gigantic data sets, and an exhaustive multiscale description of observations. We will then face the challenge of handling the complexity of the contextual and infinitely dynamic integration of processes that are the essence of living behavior.

Both international projects engage scientific policies with diverse objectives and investments in basic sciences. My hope is that the community will have the wisdom to define new standards of macromanagement and construct scientific strategies that bind together the two initiatives. To understand and simulate the autonomy and the power of abstraction of human cognition, we need to integrate knowledge from the wealth of structural and functional data and go beyond bottom-up functional genomics.

We are not yet well armed for this: current interpretations of brain function are governed by principles from the past centuries, if not from Aristotelian times. Big Science is nowadays driven by technical prowess, but there is no definitive conceptual model of the Brain. Above all, we need new concepts to understand the neural code and build falsifiable models.

Social Scientific Revolution

Zachary F. Mainen
Champalimaud Neuroscience Programme

The U.S. and European brain initiatives reflect growing societal concern about mental illness and attempts to spur solutions through directed investment. The focus on technology development, rather than on mental illness per se is perhaps a surprising consensus but a wise one. Historically, attempts to promote cures to complex diseases have yielded unmet goals, notably in the "war on cancer." But well-defined "engineering" projects have succeeded and leveraged further discovery, as with the Human Genome Project. While neuroscience has garnered much fundamental knowledge, we face more complex problems than anything tackled scientifically before. We are still in an age of exploration not exploitation. To cure complex brain malfunctions, we will need to leverage still more discoveries. And these will likely be facilitated by new technologies to monitor and model brain function, as promised by the brain initiatives. But I would wager that instrumentation and simulation may not be enough. Solving the brain will also require truly new forms of scientific collaboration and collective discovery. Social media (Facebook, Twitter, etc.) have profoundly impacted social lives and geopolitical events but have yet to transform science. In the brain initiatives, one can see the seeds of such a "social scientific revolution". But a concerted effort to foster better social technologies for science may be in order. The much-anticipated neuroscientific "spring" might actually depend on it.

The Other Half

Jennifer Raymond
Stanford University

I teach a graduate seminar where we train the next generation of neuroscientists to design experiments to uncover principles of brain function. For most of the course, students design experiments constrained by existing technologies. But at the end of the course, we encourage them to dream big and imagine what they would do if they had the ability to measure anything they wanted about the brain—every molecule, structural detail, and electrical signal of every neuron. As students engage in this exercise, they quickly realize that better experimental tools and more data cannot replace the need for thoughtfully designed experiments to address specific questions. Supporters of the Obama/NIH and European brain initiatives must likewise recognize that the tools and databases they are promising are only half of the solution. We also need scientists who can skillfully apply such tools to specific questions about how neural circuits function. Unfortunately, scientists with this expertise are now struggling to survive low research-funding levels, and talented young scientists are seeing this and rejecting research careers because they don't seem like a viable option. Thus, the success of the "big data" brain initiatives in accelerating discovery and cures will depend entirely on whether they are accompanied by improved support for investigator-initiated, hypothesis-driven research. Investment in better hammers will not pay off if the skilled carpenters go out of business.

Moving Parkinson's

Tom Isaacs
The Cure Parkinson's Trust

Since first being diagnosed with Parkinson's some 20 years ago at the age of 26, my resolve to see improvements in the treatment of Parkinson's has become as all-consuming as the condition itself. During this time, my initial concern for my personal well being shifted to dismay at the misery that Parkinson's causes some 6 million people around the world and the unnecessary barriers which stand in the way of possible breakthroughs in treating the condition. I have no doubt about the potential for scientific advances to dramatically improve Parkinson's treatment, but the combination of bureaucracy, an increasingly risk averse pharmaceutical industry, and a general dearth of investment in the sector has meant that the progress made in Parkinson's has been about as dynamic as I am in the morning without my medication.

For those of us who have Parkinson's, there is an urgent need for those in power to unlock the shackles of neuroscience. Now is the time to release the vast potential of progress in scientific understanding and to allocate resource so that these advances can make an impact on the actual lives of those who live with this condition.

My hope is that the current international investments in brain research will prioritize collaborations between government, industry, and academic scientists that will enable kinds of breakthroughs in Parkinson's that I know we are poised to make.